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EXAMINER

PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
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1645

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

09/732,091

Applicant(s)

TIAN ET AL.

Examiner

Ginny Portner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 89-159 is/are pending in the application.
- 4a) Of the above claim(s) 93,100-124 and 135-159 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 89-99 and 125-134 is/are rejected.
- 7) ☒ Claim(s) 94-99 and 129-134 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

New Claims 89-159 are pending; all other claims have been canceled.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 26, 2006 has been entered.

Rejections Withdrawn

2. In light of the cancellation of all of the prior claims, the rejections are withdrawn.

Election/Restrictions

3. Newly submitted claims 93, 101-124, 135, 136-137, 139-149, 159 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

4. The originally elected invention was directed to the 30 Kda polypeptide, and not fragments/derivative polypeptides nor combination compositions that comprise additional specific antigens recited in claim 93.

5. While the finally rejected claims recited the phrase "or a HP30-derived polypeptide", this species of invention was withdrawn from consideration, and not examined in light of the responses made on pages 2-3 of the Office Action mail dated April 26, 2005 that stated embodiments directed to fragments would not be rejoined, nor examined. Applicant's definition of HP30-derived polypeptide at page 15, is directed to fragments, see page 15, lines 1-11. This embodiment has not been examined, was withdrawn from consideration and was not elected by Applicant for consideration in response to the original election/restriction requirement.

6. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 93 and 100 (combination composition not previously examined), 101-124 (HP30 fragment/derived compositions, defined at page

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15, paragraph 1-2 of the instant Specification to be a fragment of HP30), 135 (combination composition with HP56, not previously examined), 136-159(HP30 fragment/derived compositions) are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

7. Claims 89-92, 94-99, 125-134 are under consideration in so far as the claims read on the elected finally rejected species of invention directed to compositions that comprise a 30 kDa polypeptide of *Helicobacter*.

8. It was noted that the finally rejected claims recited SEQ ID NO 4 or the coding sequence for SEQ ID NO 4, which is SEQ ID NO 3, and all of the claims no longer recite these SEQ ID Nos..

Specification

9. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

10. The hyperlinks and/or other form of browser-executable codes are found at page 11, line 27 and page 13, line 22. They must be removed.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 89, and 91-92 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 7-9 of U.S. Patent No. 5,897,475.

Although the conflicting claims are not identical, they are not patentably distinct from each other because

13. The allowed claimed compositions were defined to be produced from Deposited strain G1-4 (allowed claim 9) which were inactivated (allowed claim 4), inactivated includes compositions of H.pylori G1-4 sonication inactivated cells ('475, col. 9, line 59 and lines 50-62), which comprises HP30 polypeptide being isolated from H. pylori strain GI-4,

14. The term "isolated" defined in the instant Specification (page 21, paragraph 1) means that the product is significantly free of other biological materials with which it is naturally associated". The inactivated H.pylori GI-4 sonicated cells were combined with an adjuvant (allowed claim 7, defined to include) and a pharmaceutically acceptable diluent (see allowed claim 3).

15. The combination of reagents being the inactivated GI-4 sonicate together with an adjuvant and diluent is defined in US Pat. 5,897,475 (col. 9, lines 34-50) and claimed in allowed claims 1-4, and 7-9.

16. The instantly claimed compositions (instant claim 89, 91-92) that comprise an isolated HP30 polypeptide in combination with other immunogens in a mixture of lipids, lipoproteins, phospholipids, proteins, lipooligosaccharides (instant claim 92) reads on the

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allowed whole inactivated cell sonicate of G1-4 (allowed claims 4, 8-9) of US Pat. 5,897,475).

17. The allowed claims define an obvious species in the instantly claimed genus of compositions that comprise an adjuvant, carrier or diluent together with an HP30 polypeptide, in mixture of proteins, lipoproteins, phospholipids, lipooligosaccharides, lipids and lipoproteins from any source (Instant claim 92 and allowed claim 4). The allowed inactivated sonicate being a combination of H. pylori strain G1-4, polypeptides together with H.pylori G1-4 lipids, lipoproteins, phospholipids, proteins, lipooligosaccharides. The allowed inactivated (sonicate by definition) composition (allowed claim 4) of H.pylori strain G1-4 reads on the instant compositions that also comprise an adjuvant (pending claim 1 and allowed claim 7) and a carrier (pending claim 91 and allowed claim 3).

18. The allowed species claims anticipate the instantly claimed genus of compositions that encompasses compositions produced from H.pylori strain G1-4 (allowed claim 9), in combination with lipids, lipoproteins, phospholipids, proteins, lipooligosaccharides from any source. The allowed inactivated sonicate composition of Helicobacter G1-4 that comprises an adjuvant in combination with a diluent/carrier anticipates the instantly claimed invention as now claimed.

Claim Objections

19. Claim 94, 95-99, 129, 130-134 are objected to because of the following informalities:
 20. Claims 94 and 129 recite various abbreviations, the meanings of which are unclear. The recitation of abbreviation in the claims is permitted upon their definition at their first appearance (ie claim 94).
 21. Claims 95 and 130 recite the phrase "adjuvant or mixture of adjuvants is mLT"; the claims recites a single adjuvant "mLT" which is not a mixture of adjuvants. The combination of claim limitations is not internally consistent in tense (singular vs. plural tenses).
 22. Claims 96 and 131 recite the phrase "adjuvant or mixture of adjuvants is alum"; the claims recites a single adjuvant "alum" which is not a mixture of adjuvants. The combination of claim limitations is not internally consistent in tense (singular vs. plural tenses).
 23. Claims 97 and 132 recite the phrase "adjuvant or mixture of adjuvants is AB5"; the claims recites a single adjuvant "AB5" which is not a mixture of adjuvants. The combination of claim limitations is not internally consistent in tense (singular vs. plural tenses).
 24. Claims 98 and 133 recite the phrase "adjuvant or mixture of adjuvants is CFA"; the claims recites a single adjuvant "CFA" which is not a mixture of adjuvants. The combination of claim limitations is not internally consistent in tense (singular vs. plural tenses).
 25. Claims 99 and 134 recite the phrase "adjuvant or mixture of adjuvants is alum and AB5"; the claims recites a mixture of adjuvants "alum and AB5" which is not a single adjuvant but a mixture. The combination of claim limitations is not internally consistent in tense (singular vs. plural tenses). Appropriate correction is required.

Claim Rejections - 35 USC § 112

26. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

27. Claims 125-127, 129 and 131, 134 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.
28. The claimed methods are directed to methods that reduce or prevent colonization of *Helicobacter* spp, by administering only HP30 polypeptide (claims 125-127) or HP30 together with alum (claim 131) or HP30 together with LT and alum (claim 134).
29. The instant Specification at page 70, Table 3, and Figure 9 show that HP30 is able to reduce infection relative to a control without co-administration of an adjuvant (Figure 9) but not prevent infection without HP30 being administered subcutaneously together with CFA adjuvant (see Table 3, page 70, rHP30 + CFA "0" stomach culture CFU/ml; page 70, paragraph 2).
30. The instant Specification does not show data for reduction or prevention of colonization when HP30 when combined only with mLT, QS21, MF59, CpG DNA, PML, calcium phosphate, or PLG (instant claim 129). While it is clear that an immune response would be stimulated, the effect of the immune response relative to the claimed method of reducing or preventing infection is not described/disclosed.
31. The combination of rHP30 + alum (Table 3, page 70 and Figure 9) and HP30 + (LT and alum, Figure 9) did not prevent infection, but reduced the number of colonies

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relative to a negative control and therefore these compositions are not enabled for preventing infection in light of the data presented in the instant Specification.

32. Figure 9 shows the administration of HP30 alone only reduced the number of colonies, and did not prevent infection (see figure 9, instant Specification).

The Wands factors to be considered:

.the quantity of experimentation necessary : undue, due to the fact that any type of animal, any amount, any mode of administration, with or without various adjuvants must be tried to determine what will work and what will not work, in light of the unpredictability of compositions that comprise HP30 shown by the data provided in the instant Specification, and the knowledge in the art that *Helicobacter* vaccines are unpredictable.

.the amount of direction or guidance presented : specific embodiments shown, but additional experimentation needed for others in order to determine the claimed biological function of preventing infection with of the HP30 compositions when administered to an animal with or without an adjuvant.

.the presence or absence of working examples; yes, some compositions worked and other did not work (see Table 3, figures and Examples)

.the nature of the invention: compositions requiring the induction of complex immunological responses which serve to prevent living pathogenic *Helicobacter* strains of bacteria from colonizing any animal.

.the state of the prior art; defines *H.pylori* vaccines that prevent infection to be unpredictable, though highly immunogenic.

.the relative skill of those in the art: high with respect to general methods, but knowledge of whether a single immunogenic *Helicobacter* protein will serve to reduce or prevent infection must be determined on a case by case basis.

.the predictability or unpredictability of the art; vaccines are unpredictable in light of Monath et al (1994) that shows *Helicobacter pylori* compositions are not protective, while highly immunogenic (see page 1383, col. 2, bottom half of paragraph); Boslego et al (page 21, col. 2) provides evidence that highly immunogenic, conversed proteins are not predictably vaccine compositions (see col. 2, p. 2 "no apparent protection" against the heterologous strain; col. 2, p. 3 "There was no vaccine protection despite the development of high levels of serum cross-reactive pilus antibody levels"); Ellis teaches "The key to the problem is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies, such antibodies having the capacity to neutralize infectivity and thus protect the host against attach by the pathogen(see page 571, col. 1, p. 3); Dunkley et al (1991) teaches the mode of administration of *H.pylori* immunogenic composition is essential to development of significantly enhance immune responses (see paragraph 3); Heap et al parenterally administered *H. felis* to an animal and f found that this mode of administration "gave absolutely no protection against gastric colonization (last paragraph). Aebischer et al (2005) states that important issues still need to be resolved before an *H.pylori* vaccine

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will become a reality (abstract, last sentence).

.breadth of the claims : broad but not indefinite.

33. Therefore, claims 125-127 and 131 and 134 are not enabled for preventing infection in light of the data presented in the instant Specification which shows the criticality of the presence of CFA adjuvant together with HP30, administered subcutaneously to prevent infection (Table 3, page 70).

34. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35. Claims 97 and 99 recites the limitation "AB5" in dependence upon claim 94, which does not recite this term. There is insufficient antecedent basis for this limitation in the claim.

36. Claims 132 and 134 recites the limitation "AB5" in dependence upon claim 129, which does not recite this term. There is insufficient antecedent basis for this limitation in the claim.

37. Claims 125-134 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

38. Claims 125-134 recite the phrase "effective amount". The common phrase "an effective amount" may or may not be indefinite. The proper test is whether or not one skilled in the art could determine specific values for the amount based on the disclosure. See *In re Mattison*, 509 F.2d 563, 184 USPQ 484 (CCPA1975). The phrase "an effective amount . . . for growth stimulation" was held to be definite where the amount was not critical and those skilled in the art would be able to determine from the written disclosure, including the examples, what an effective amount is. *In re Halleck*, 422 F.2d 911, 164 USPQ 647 (CCPA 1970). The phrase "an effective amount" has been held to be indefinite when the claim fails to state the function which is to be achieved and more than

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one effect can be implied from the specification or the relevant art. In re Fredericksen 213 F.2d 547, 102 USPQ 35 (CCPA 1954). The claims should be amended to define the function for the amount administered to be an amount that produces an immune response, or to induce a protective immune response; or an equivalent phrase for which the instant Specification provides original descriptive support.

Claim Rejections - 35 USC § 102

39. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

40. Claims 89, 91, 125, 126, 127, 128 are rejected under 35 U.S.C. 102(e or b) as being anticipated by Bolin et al (US Pat. 6,025,164 or WO96/38475 ('164 is a 371 of WO96')). Please note, all sites are from the US Patent document but are also present in the 371 document.

Bolin et al disclose the instantly claimed invention directed to compositions comprising a *Helicobacter pylori* polypeptide of about 30 Kda, wherein the polypeptide is combined with an adjuvant. The polypeptide of Bolin et al was identified with a monoclonal antibody designated HP30 (see '164, col. 1, line 57 and col. 8, lines 48-60).

Bolin et al disclose the polypeptide together with an adjuvant (see col. 6, lines 34-38) formulated into nasal and subcutaneous compositions and methods that comprise the step of administering (see '164 col. 6, lines 32-36) an immunologically effective amount (see '164, col. 7, line 12) of the polypeptide together with an adjuvant and carrier (see '164, col. 6, lines 27-38; col. 16, section 8.2.2) to an individual (see '164 col. 5, lines 62-67, especially, line 64 "mammal, including humans").

One method disclosed administered the HP30 immunoreactive polypeptide with a mucosal adjuvant to a mammal (see '164, col. 16, section 8.2.2), and concludes that the polypeptide is able to reduce the degree of colonization of *H. pylori* (see col. 16, lines 27-36). Bolin et al anticipates the instantly claimed invention directed to an HP30 polypeptide together with an adjuvant, and methods of administration as now claimed.

41. Claims 89-91, 92, 94-97, 125-130, 131-132 are rejected under 35 U.S.C. 102(b) as being anticipated by Lissolo et al (WO97/12909) in light of the English translation of PCT WO97' 371 document (PG-Pub 2002/0151462).

42. Lissolo et al (WO97/12909) disclose the instantly claimed invention directed to compositions comprising

Instant claims 89-90: a *Helicobacter pylori* polypeptide of 30 Kda (see WO97' Figure 4, frame A, abstract, page 2, line 24; page 4, lines 27-34 and PG-Pub [0009]; [0028-0035]), which is also present in *H. felis* and other *Helicobacter* species (see WO97', page 7, lines 8-10 and PG-Pub, [0049]) wherein the polypeptide is combined with an adjuvant, wherein the adjuvants include:

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Instant claims 92, 94, 95, 96, 97: (, Arg192Gly LT mutant (mLT, AB5), aluminum hydroxide (alum) and major bacterial lipopolysaccharide (PML) (see adjuvant WO97', page 11, paragraphs 1-5; PG-Pub, [0062-0066]), together with

Instant claim 91: a diluent carrier (see WO97', page 12, paragraph 1-2; PG-Pub [0068-0069])

Instant claims 125-130, 131-132 : Lissolo et al disclose the polypeptide together with an adjuvant formulated into nasal and subcutaneous compositions (see WO97' page 10, paragraph 3; PG Pub [0060]) and methods that comprise the step of administering an immunologically effective amount (see WO97, page 12, p. 1; PG-Pub [0067]) of the polypeptide together with an adjuvant and carrier to an individual (see WO97', page 11, paragraph 6 and page 12, paragraph 1; PG-Pub [0067]) by a nasal or subcutaneous route of administering.

Lissolo et al anticipates the instantly claimed inventions as now claimed.

43. Claims 89,91, 92 (reads on protein/inactivated whole cell/attenuated organism adjuvants), 94 (alum, hLT, mLT, CFA (Freund's adjuvant)), 95-98, and method claims 125-133 are rejected under 35 U.S.C. 102(b) as being anticipated by Pace et al (WO96/11257 (1996)).

Please Note: The examiner is reading the term "isolated" in light of the definition provided in the instant Specification which is "the term "isolated" means that the product is significantly free of other biological materials with which it is naturally associated" (page 21, paragraph 1, section 5.3, instant Specification), the claimed HP30 polypeptide defined to include isolation from H. pylori strain GI-4.

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Pace et al disclose the instantly claimed invention directed to compositions that comprises:

Instant claim 89: *Helicobacter pylori* G1-4 (see WO96, page 14, paragraph 1 and claim 10) polypeptides present in an inactivated (see WO96, claim 16; see WO96' vaccine (see pages 65- 68, claims 7, 10, 12 14, 15, 16, 19 and 25, especially claims 14-16, 19 and 25)

whole cell sonicate (see page 16, line 32), which would be a composition comprising all of the antigens present in the whole, but would be separated from other biological material with which it is naturally associated due to the disruption of the whole cell by sonication.

wherein the inactivation is defined to be by physical sonication resulting in a whole cell lysate (see WO96', page 14, line 35) which isolates the "proteins", "surface proteins", lipopolysaccharides, carbohydrates" from cellular components disrupted by the sonication process.

Instant claim 91: The compositions are combined with an adjuvant and a pharmaceutical carrier or diluent (see page 16, line 9 "inactivated", line 10 "adjuvant", lines 15-16 "carriers")

Instant claims 92, 94-98: The adjuvants of Pace et al are defined to include "alum, oil-water emulsion, heat labile toxin from enterotoxigenic *E.coli* (LT) nontoxigenic forms thereof (eg mLT) and/or individual subunits thereof, Bacille Calmette-Guerin (BCG), or Freund's adjuvant (see page 16, paragraph 2)" mLT being a protein toxin of *E.coli* of the form AB5 (one A subunit together with 5 B subunits) .

Instant claims 125-133: The vaccine compositions are disclosed and administered in methods of stimulating an immune response that prevents, attenuates or cures

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Helicobacter infections or diseases in the animals, the methods comprising the step of administering (see page 70, claim 25) to a mammal or bird (see page 16, paragraph 1) by local, mucosal or systemic administration which includes implant (see page 17, lines 26-28), intranasal (see page 17, line 24) and subcutaneous (see page 17, line 23) the vaccine compositions. The amount administered is an effective amount for "producing an immune response in a subject (see paragraph bridging pages 16-17). The preferred vaccine composition being one that is inactivated whole bacteria (see page 17, lines 12-13), which is defined to include whole cell sonicates which results in isolated polypeptides of G1-4, the same source of the instantly claimed Helicobacter polypeptide.

Pace et al inherently anticipates the instantly claimed invention as now claimed. While Pace et al do not describe the polypeptides in the G1-4 inactivated sonicate by relative molecular weight, Pace et al produce the same or equivalent composition from the same or equivalent source as Applicant which comprises isolated polypeptides that are not in association with the biological materials they are naturally associated, as the natural associations were disrupted/inactivated by sonication and combined with an adjuvant and diluent carrier and administered to an individual animal/mammal.

Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

44. Claims 89,91, 92, 94 (alum, hLT, mLT, CFA (Freund's adjuvant), 95-98, and methods claims 125-133 are rejected under 35 U.S.C. 102(b) as being anticipated by Pace et al (US Pat. 5,897,475, issue date April 27, 1999).

45. **Please Note:** The examiner is reading the term "isolated" in light of the definition provided in the instant Specification which is "the term "isolated" means that the product

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is significantly free of other biological materials with which it is naturally associated", the claimed HP30 polypeptide being isolated from H. pylori strain GI-4.

Pace et al disclose the instantly claimed invention directed to compositions that comprises:

Instant claim 89: Helicobacter pylori GI-4 (see claim 9) polypeptides present in an inactivated (see '475, claim 4) whole cell sonicate ('475, col. 9, line 59 and lines 50-62), which would be a composition comprising all of the antigens present in the whole, but would be separated from other biological materials with which it is naturally associated due to the disruption of the whole cell by sonication. The inactivation is defined to be by physical sonication (see '475, col. 9, line 59) resulting in a whole cell lysate which isolates the "proteins", "surface proteins", lipopolysaccharides, carbohydrates" from cellular components disrupted by the sonication process.

The compositions are combined with an adjuvant and a pharmaceutical carrier or diluent (see '475, col. 9, lines 34-50 " inactivated and may further comprise an adjuvant, such as, but not limited to, alum, oil-water emulsion, heat labile toxin from enterotoxigenic E. coli (LT) nontoxigenic forms thereof (eg. mLT) and/or individual subunits thereof, Bacille Calmette-Guerin (BCG), or Freund's adjuvant and may also further comprise a suitable pharmaceutical carrier, including but not limited to saline, dextrose or other aqueous solution.) The E.coli toxin being in the form of AB5, one A subunit associated with five B subunits (heat labile enterotoxin).

The vaccine compositions are utilized in methods of stimulating an immune response that prevents, attenuates or cures Helicobacter infections or diseases in the animals, the methods comprising the step of administering to a mammal or bird (see col.

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10, lines 17-25, and Example 15, Table 20, col. 35) by local, mucosal or systemic administration which includes implant, intranasal and subcutaneous (see col. 10, lines 17-25) the vaccine compositions. The amount administered is an effective amount for producing an immune response in an individual (see col. 9, lines 62-67 and col. 10, lines 1-16). The preferred vaccine composition being one that is inactivated whole bacteria (see claim 4), which is defined to include whole cell sonicates which results in isolated polypeptides of G1-4 (deposited strain), the same source of the instantly claimed *Helicobacter* polypeptide.

Pace et al inherently anticipates the instantly claimed invention as now claimed. While Pace et al do not describe the polypeptides in the G1-4 inactivated sonicate by relative molecular weight, Pace et al produce the same or equivalent composition from the same or equivalent source as Applicant which comprises isolated polypeptides that are not in association with the biological materials they are naturally associated, as the natural associations were disrupted/inactivated by sonication and combined with an adjuvant and diluent carrier and administered to an individual animal/mammal.

Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

Claim Rejections - 35 USC § 103

46. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1. Claims 89-92, 94, 96, 125-129, 131 are rejected under 35 U.S.C. 103 (a) as obvious over Tomb et al (August 9, 1997) in view of WO96/40893 (1996). (both references of record.)

Tomb et al describe a composition that comprises a *Helicobacter* polypeptide encoded by SEQ Id NO 3, and has the amino acid sequence of SEQ Id NO 4, which is defined in the instant Specification to be a 30 Kda polypeptide with the designator HP30. Tomb et al referred to the polypeptide be a different designator, specifically HP1588 (see Tomb et al Table 2, col. 3, middle of column), and was encoded by a nucleic acid of EMBL accession number D64718 which comprises the nucleic acid for SEQ ID NO 3.

Instant claim 89: The claimed polypeptide composition was recombinantly produced HP30 polypeptide. Tomb et al recombinantly expressed the polypeptide that shares 100% sequence identity with SEQ ID NO 4, and named the polypeptide HP1588. Though the name is not HP30, it is the identical polypeptide to HP30 as it has the amino acid sequence of SEQ Id NO 4, wherein the species is *Helicobacter pylori* (see title of reference).

Instant claim 90: With respect to the species is *Helicobacter felis*, Tomb et al does not discuss *Helicobacter felis*, the polypeptide of Tomb et al has the amino acid sequence of SEQ ID NO 4, and therefore anticipates the instantly claimed *H. felis* composition that is SEQ ID NO 4 as defined in the instant Specification.

Instant claims 92: The composition of Tomb et al further comprised one or more immunogens, wherein Tomb et al describes the expressed the *H. pylori* HP30 polypeptide to have been expressed in an *E. coli* laboratory strain of bacteria, a type of attenuated organism, a type of carrier for the recombinantly expressed HP30 polypeptide (see

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transcription and translation page 541, col. 1, paragraphs 2), which E.coli strain expresses additional immunogens that are lipids, lipoproteins, proteins.

Tomb et al describes a composition that comprises an HP30 polypeptide which has the amino acid sequence of SEQ Id NO 4, the polypeptide having been recombinantly expressed, the composition comprising one or more additionally immunogens associated with the host cell E.coli a type of carrier, but differs from the instantly claimed invention by failing to show the polypeptide together with a pharmaceutically acceptable carrier and one or more adjuvants and a method that comprises the step of administering an effective amount to individual .

WO96/40893 show a polypeptide that shares identity with SEQ Id NO 4 (wo96 refers to the polypeptide as accession umber AAW20486) and is encoded by a sequence of SEQ ID NO 3, and teaches compositions that comprise Helicobacter polypeptides together with a pharmaceutically acceptable carrier and an adjuvant (see page 84, paragraphs 4-5 and page 85, paragraphs 1-4, specific adjuvants described include polylactide glycolide (PLG, page 85, line 35), aluminum hydroxide (alum, page 85, line 11), heat labile E.coli toxin (LT, see page 85, line 21), QS21 (saponins, page 85, line 22) in an analogous art for the purpose of formulating and administering compositions that comprise an effective amount (see all claims, to include claim 99, page 1471) of H. pylori polypeptide for the purpose of (subcutaneous, see page 85, line 2; intranasally (pulmonary, page 85, line 5) inducing an immune response (see page 85, last line) to H.pylori polypeptides; H.pylori being a known human pathogen associated with gastric ulcer disease and gastric adenocarcinoma (see page 1, lines 5-17).

It would have been obvious to the person of ordinary skill at the time the invention was made to modify the composition of Tomb et al with the carrier and

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adjuvant of WO96' because both references are directed to polypeptide compositions of *H.pylori* that comprise an amino acid sequence of SEQ ID NO 4, and WO96' suggests, teaches and provides guidance for the formulation of polypeptide containing compositions that further comprise a pharmaceutically acceptable carrier and an adjuvant (see WO96' pages 84-85) because WO96' teaches the importance of inducing an immune response to a known human pathogen associated with severe disease, wherein induction of an immune response to the compositions results in the attainment of an antibody reagent for diagnostic and therapeutic purposes (see page 2, lines 18-19 and page 85, lines 37-39 and first paragraph on page 86).

In the absence of a showing of unexpected results, the person of ordinary skill in the art would have been motivated by the reasonable expectation of success of obtaining compositions that comprise a polypeptide, carrier and adjuvant because WO96 teaches compositions that comprise *Helicobacter* polypeptides together with a pharmaceutically acceptable carrier and an adjuvant (see page 84, lines 26-34) and Tomb et al and WO96' are both directed to the formulation of compositions that will serve in inducing an immune response which can serve as a tool for gaining greater insight into the pathogenesis of *H.pylori* (see WO96', page 83, paragraphs 2-4), as well as vaccine development (see Tomb et al, page 539, col. 1, last line; see WO96' abstract) and WO96' teaches through incorporating the *Helicobacter* polypeptide (see WO96', page 84, last paragraph, first line) into a composition that comprises both a carrier to protect the antigen (see WO96' page 85, lines 32-33) from acidic environments and an adjuvant to obtain an enhanced immune response to the polypeptide, an immunogenic composition

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can be readily obtained. Tomb et al in view of WO96' (alignment provided herewith) obviates the instantly claimed invention.

Conclusion

2. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US006083683A US006051416A US006077678A US005976525A US2001/0010821 US20020151462A1 US20020146423A1 US 20040033240A1 and US 20040138415A1 are cited to show Helicobacter compositions.

3. Bolin (1995) is cited to show a H.pylori surface exposed protein that immunoreacts with a monoclonal antibody designated HP30.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Vgp

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